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Overview of Structure Activity Relationship and Binding Affinities of Angiotensin Receptor Blockers (ARBs)

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Background: Ang II is a vasoconstrictive peptide hormone that shows a wide variety of physiological actions. Ang II is the primary cause of inducing hypertension. In order to deal with hypertension ACE inhibitors and ARBs are used worldwide. These ARBs exert action by blocking the binding of Ang II on AT1 receptor. Peptide ARBs are rarely used as compared to non-peptide due to low bioavailability, short duration of action and partial agonistic activity. Moreover, the structure activity relationship played an important role in designing the more potent ARBs.

Methods and Preliminary results: The data for the SAR of ARBs is compiled from the literature available. It has been seen that the basic pharmacophore of ARBs should have a heterocyclic ring system, an alkyl side chain and an acidic group on the biphenyl ring. All the groups which are forming the pharmacophore are responsible for the binding of the compound to the Angiotensin receptor. The higher binding affinity of the Irbesartan is because of the cyclopentyl group present in Irbesartan which forms Hydrophobic interaction with the Hydrophobic pocket of AT1 Receptor whereas the good binding affinity of the Telmisartan also can be explained by the COOH group present at the 2 position of Biphenyl methyl group where as other ARBs contain tetrazole group. On the other hand Valsartan represents a nonheterocyclic AT1 Receptor selective antagonist in which the imidazole of losartan has been replaced by an acylated amino acid. The acylated amino acid leads to higher binding affinity of Valsartan.

Preliminary conclusion: It has been concluded that the small modification/difference in molecular structure of the ARBs changes the binding affinity of the various ARBs and hence affects the efficacy and potency of a particular ARBs.